

Please consider the following remarks in support of the revised claims and in connection with rejections under 35 USC 112 and 35 USC103:

#### **REMARKS**

The enablement requirements (35 USC 112) have been addressed in amended claim 1 and original claim 2. The inventors are medical doctors in ophthalmology and have observed such effects in practice for patients using the combination of say nitroglycerine for heart problems and Viagra (sildenafil citrate) for erectile dysfunction and have observed substantial lowering of intraocular pressure in the eye of such patients. No data was reproduced in the specification in this regard for privacy reasons. All segments described in claim 2 are depicted in paragraph 0030 of the detailed description in the specification and thus such subject matters are covered in the specification.

The obviousness rejection under 35 USC 103 is now addressed. The essential reason for rejection of basic claims by the examiner is that the combination of NO donors and cGMP-PDE5 inhibitors to heal glaucoma is obvious to one skilled in the art, because Nathanson in 1992 (Journal of Pharmacology) teaches NO donors as hypotensive agents for glaucoma and in 2002, Laties (EP 1 074 258 A2) teaches various cGMP-PDE5 inhibitors and in particular Sildenafil Citrate as treatment agent for glaucoma. We would like to address these issues and present reasons to the examiner that these rejections can be overcome. First in connection with Nathanson, we do agree that NO donors are hypotensive. However, our disclosure combines NO donors with cGMP-PDE5 inhibitors to enhance the effect of NO donors. WE have observed substantial synergistic effect of combining the two. Please refer to our sections 0009 and 0023 amongst others for detailed discussions on these issues. To simply argue it, cGMP-PDE5 does not by itself lower the ocular pressure and is not a hypotensive agent despite Laties claims, because it is not a vasodilator. All it does is that it inhibits the formation of enzyme PDE5 that specifically destroys enzyme cGMP, which is a vasodilator, produced by NO donors. These are fully explained in our disclosure and in particular sections 0009 and 0023 of detailed description. This synergistic combination was not obvious to Professor Nathanson in 1992 (Journal of Pharmacology), as the examiner has noted. However, Laties knew this combination but he chose not to claim it. Laties in column 1, (section 005) and column 2, (section 0008) indicates that he is aware of the effect of NO donors in lowering IOP but maintains that he does not want to use NO donors in combination with cGMP-PDE5, because they make glaucoma worse (column 2, line 31-32 actually claims the combination works against glaucoma and glaucomatous optic neuropathy). Therefore, he intentionally avoids the combination of NO donors and cGMP-PDE-5 inhibitors and does not claim it. However, our observations of patients have indicated that the combination actually works very well as reported above. We must emphasize the fact that cGMP-PDE5 inhibitors do not act as vasodilators which is needed to treat glaucoma in order to dilate the Schlem's canal for enhanced aqueous humor drainage and lowering of IOP. All they do is to inhibit the formation of enzyme PDE5 that destroys cGMP enzyme (produced by NO donors) that

causes vasodilation and treatment of glaucoma. Therefore, Laties claims are not really justified by experiment. The reason why cGMP-PDE5 in the form of Viagra works as erectile enhancer is not because it does vasodilation for erection and enhanced blood flow to the penis, but because it slows down the destruction of cGMP enzyme produced naturally by the body when arousal occurs by the enzyme PDE5 produced by the body to suppress it. In patients with glaucoma no such natural production of cGMP in the ophthalmic area (eye) is documented and thus using Viagra for glaucoma will not work by itself and there is no published document proving that. Laties is misled by the erectile dysfunction treatment effects of Viagra and assumes that the same will happen for glaucoma, namely vasodilation. We respectfully ask the examiner to consider our intricate medical points in this discussion and do not consider the NO donor+cGMP-PDE5 as an obvious issue.

Having responded to each and every objection and rejection raised by the Examiner, it is believed that the patent application is now in condition for allowance, and such allowance is respectfully requested. If the Examiner has any questions or suggestions for expediting an allowance in this matter, the Examiner is invited to call the undersigned collect.

The Commissioner is authorized to charge any required fees, which may be required during the entire pendency of the application.

Respectfully submitted,

Dated: October 4, 2005

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